

# To Study The Percentage of HIV Seropositivity in Smear Positive Tuberculosis Cases.

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## ABSTRACT

**Background:** Tuberculosis is the commonest opportunistic infection and the leading cause of death in HIV patients in developing countries and accounts for about 40% of all manifestations seen in HIV patients. Correct diagnosis and treatment of tuberculosis helps to reduce burden of TB. However there are difficulties in achieving this goal such as difficulties in diagnosing tuberculosis in HIV infected patients due to unusual clinical picture with increase in smear negative AFB pulmonary tuberculosis and atypical findings on chest radiography. There is a paucity of literature regarding determination of percentage of HIV seropositivity in smear positive tuberculosis cases in Northern India. Hence, this study was planned to study the correlation and burden of HIV seropositivity in smear positive tuberculosis cases. **Methods:** A prospective study was conducted at the Chest and TB hospital, Amritsar which included 150 smear positive tuberculosis cases. HIV seropositivity was determined in all the patients. **Results:** In our study, the HIV seropositivity detected in 150 smear positive tubercular cases was 3.33% which is more than the prevalence seen in most of the northern states and lower than the southern and north eastern states of India. **Conclusion:** The HIV seropositivity detected in 150 smear positive tubercular cases was 3.33% which is more than the prevalence seen in most of the northern states and lower than the southern and north eastern states of India.

**Keywords:** Tuberculosis, Human Immunodeficiency Virus, CD4 cells.

## INTRODUCTION

Tuberculosis, known to mankind since ages, is an infectious bacterial disease caused by *Mycobacterium tuberculosis* that spreads almost exclusively by the respiratory route, primarily involving the lungs. HIV infection, on the other hand, acquainted to man in the last decades of the last century only, is a viral disease, spreads by various routes and is notorious for causing immune suppression in the body. The dual epidemic of tuberculosis and HIV is a significant problem in the developed and developing countries. The HIV pandemic has altered both the epidemiology of tuberculosis and the measures for approaches to its control. WHO estimates that more than 7 million

people, 98% of whom are in the developing world, are co-infected with HIV and tuberculosis.<sup>[1]</sup> An estimated 920 000 people living with HIV (PLHIV) worldwide fell ill with TB in 2017. TB is the leading cause of death among people with HIV, accounting for some 300,000 people who died from HIV-associated TB in 2017. Globally, PLHIV were 20 times (17 – 23) more likely to fall ill with TB than those without HIV in 2017. PLHIV face the threat of drug-resistant TB. If diagnosis is delayed, there is increased risk of mortality from multidrug-resistant and extensively drug-resistant TB.<sup>[2]</sup>

Routine HIV testing should be offered to all patients with presumptive and diagnosed TB. Globally in 2017, 60% of new and relapse TB patients (3.8 million) had a documented HIV test, up from 58% (3.6 million in 2016). Routine screening for TB symptoms of all PLHIV is essential for ensuring early detection. Scale-up of the latest algorithms and WHO-recommended rapid diagnostics such as Xpert MTB/RIF and lateral flow urine – lipoarabinomannan assay (LF-LAM) are also crucial

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for fast-tracking early diagnosis and treatment. 8% of PLHIV newly enrolled in HIV care in 92 countries were notified with TB in 2017.<sup>[2]</sup>

The 30 high TB burden countries accounted for 87% of all estimated incident cases worldwide, and eight of these countries accounted for two thirds of the global total: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%) and South Africa (3%).<sup>[3]</sup> HIV prevalence among incident TB patients is estimated to be 4.00%. 87,000 HIV associated TB patients are emerging annually. By numbers, India ranks 2nd in the world and accounts for about 10% of the global burden of HIV-associated TB. The mortality in this group is very high and every year, 12,000 people die every TB/HIV co-infected patients.<sup>[4]</sup>

HIV infection reduces the number and functionality of CD4+ T helper lymphocytes that direct and coordinate acquired immunity against most pathogens.<sup>[5]</sup> The decrease in CD4+ T lymphocyte count leads to various Opportunistic Infections (OI) in HIV infected persons.<sup>[6]</sup> Opportunistic respiratory tract infections are common and remain a major cause of morbidity and mortality in HIV patients. In developing countries, patients are usually unaware of their HIV status until they are tested on presentation with symptoms suggestive of this infection. It is estimated that 65% of the patients infected with HIV present with pulmonary involvement as their first clinical manifestation, and that approximately 80% of HIV positive patients have some kind of pulmonary involvement over the course of the disease.<sup>[7]</sup>

M.tuberculosis/HIV co-infection is a major public health issue in developing countries. Although most co-infections occur in sub Saharan Africa,<sup>[8]</sup> the number of co-infected patients has increased considerably in South-East Asia.<sup>[9]</sup> Tuberculosis is generally easier to diagnose early in the course of HIV infection, owing to its classical expression (such as cavitation), and AFB examination is therefore routinely performed. In the later stages of HIV disease, clinical signs are more varied because of unusual clinical and radiological features. As a result, AFB examination is often delayed, and sputum smears may be negative particularly in patients without cavitation.<sup>[9]</sup> In patients with severe immunosuppression, the mycobacterial burden may be very high and disseminated. For this reason, *Mycobacterium tuberculosis* can be found in sputum, blood and others organs.<sup>[10]</sup>

AFB-negative tuberculosis is less of a public health problem because it is less contagious, even though this form of tuberculosis is still responsible for 15 to 20% of cases of human-human transmission.<sup>[11]</sup> In individual patients coinfecting by HIV, AFB negative tuberculosis is associated with a high mortality rate, because of delayed access to antituberculous treatment and the high degree of underlying

immunodepression.<sup>[12]</sup> Thus, AFB-negative patients pose a therapeutic dilemma: deciding to treat on clinical grounds alone may mask the real cause of clinical manifestations, carries a risk of unnecessary toxicity and can interfere with antiretroviral therapy, yet failure to treat carries a risk of death from tuberculosis and of persistent infectivity.<sup>[11]</sup>

The annual risk of developing TB disease in a PLWHA who is co-infected with *M. tuberculosis* is 5 to 15 percent.<sup>[13]</sup> HIV increases the rate of recurrent TB disease, which may be due to either endogenous reactivation (true relapse) or exogenous re-infection.<sup>[14]</sup> Increase in tuberculosis cases amongst the PLWHA poses an increased risk of TB transmission to the general community.

As per RNTCP guidelines, CNAAT is the preferred diagnostic technique for TB testing in PLHIV when compared to smear microscopy. Sputum microscopy has poor sensitivity in detecting TB in PLHIV due to fewer organisms in sputum. In addition to diagnosing TB, there is also the need to test for drug resistance so as to provide the most effective treatment to curb the progress of drug-resistance TB (DR-TB) in patients and also to reduce risk of transmission in the community.

## MATERIALS AND METHODS

The present study was conducted after approval from the institution's ethical committee and informed consent of the patient in the department of Tuberculosis and respiratory diseases, Government medical college, Amritsar.

### **Study population**

The study included 150 patients of pulmonary tuberculosis who were diagnosed positive by smear method coming to outpatient department or admitted in wards of the various departments of Government Medical College Amritsar, Chest and TB Department and ART centre Amritsar.

### **Inclusion criteria:**

1. Patients having sputum smear positive pulmonary tuberculosis.
2. Patients having sputum smear positive tuberculosis with extrapulmonary involvement.
3. Patients who consent to join the study.
4. Age should be between 15-70 years.

### **Exclusion Criteria**

1. Sputum smear negative pulmonary tuberculosis patients.
2. All patients who do not consent to join the study.

### **Methodology:**

All patients those met the inclusion criteria were assessed. A pre-structured proforma was filled in those cases which were included in the study.

A. The patients were assessed on parameters such as sputum microscopy at time of initiation of therapy. All the sputum samples were processed under fluorescent staining method.

B. Testing of the cases for Human immunodeficiency virus-1 and human immunodeficiency virus-2 were done by COMBAIDS-RS Advantage-ST (HIV 1+2 immunodot test kit), SD Bioline HIV-1/2 test and Trispot AIDS Scan. All the tests were performed according to the instructions provided in the kits supplied by NACO.

C. History, general physical and respiratory examination, contact history, past history of ATT(anti-tubercular therapy) intake, history of any addiction, ESR, CD4 Count, chest X-ray findings, etc. were also taken.

## RESULTS

The present study was conducted in the department of Chest and TB, Government Medical College, Amritsar which included smear positive tuberculosis cases coming to outpatient department or admitted in the wards. The 150 patients were registered during the study period those who met all the inclusion/ exclusion criteria. All the patients were tested for Human immunodeficiency virus-1 and human immunodeficiency virus-2. The observations and results of the studied patients were recorded and tabulated as follows:

**Table 1: HIV Status of Cases**

HIV Status	No. of Patients	Percentage
Reactive	5	3.33
Non-Reactive	145	96.67
Total	150	100.00

Out of 150 patients, 5 (3.33%) patients were diagnosed cases of HIV/AIDS. Rest all i.e. 145 (96.67%) were HIV negative.

The maximum number of patients belonged to the age group of 20-29 years i.e. 31(20.67%) cases followed by 29 (19.33%) cases in age group 40-49 years and 26 (17.33%) in >60 years age group. 23(15.33%) cases were found in age groups 30-39 and 50-59 years each and minimum patients were found in this age group only. Mean age was 39.89 years. The youngest patient was 18 years old and the oldest patient was 70 years in age.

42 (28%) patients were females and 108 (72%) were males showing a marked male preponderance. Also, the most common addiction was smoking, present in 40 (26.67%) cases of study subjects. It was followed by alcoholism which was present in 39 (26%) patients and drug abuse was present in 17 (11.33%) of cases. 13 (8.67%) cases out of 150 were occasional alcoholics.

38 (25.33%) cases were diabetic and rest i.e. 112 (74.67%) were not. Also, out of 150 tuberculosis cases, 82 (54.67) were new cases, 46

(30.67%) showed previous history of anti tubercular drugs intake and 22 (14.67%) were multi drug resistant cases. Of the 46 previously treated cases, 11 (7.33%) cases were lost to follow up cases.

**Table 2: Various Variables of HIV Seropositive Patients a). Age wise Distribution in HIV seropositive patients (n=5)**

Age (years)	No. of Patients	Percentage
20-29	2	40.00
40-49	2	40.00
50-59	1	20.00

**Table 2 b): Gender Distribution in HIV seropositive patients (n=5)**

Gender	No. of Patients	Percentage
Males	5	100.00
Females	0	0.00

**Table 2 c): Drug addiction wise Distribution in HIV seropositive patients (n=5)**

Drug Addiction	No. of Patients	Percentage
Alcoholism	3	60.00
Smoking	3	60.00
Others	3	60.00

**Table 2 d): Risk factors for possible mode of transmission in HIV seropositive patients (n=5)**

Risk factors	No. of Patients	Percentage
Heterosexual	2	40.00
Promiscuity	3	60.00
Intravenous drug abuse	0	0.00
h/o blood transfusion	0	0.00
h/o HIV seropositivity in wives	0	0.00

The above table shows the various findings seen in HIV seropositive patients detected among all smear positive tuberculosis cases. As per the table:

- The 20-29 and 40-49 age groups are equally affected.(40%)
- All the HIV seropositive cases are males (100%).
- 3 (60%) out of 5 patients were alcoholic, smokers and give history of other drug abuse too.
- 40% had histories of heterosexual relationships with more than 1 partner; 3(60%) patients were intravenous drug users and none had past histories of blood transfusion or HIV seropositivity in wives.

Also, 60% belonged to rural population (including two prisoners) and the rest 40% to urban population. 3 (60%) of them were newly detected tubercular cases while the rest two (40%) were previously treated case of which one was a lost to follow up case. 80% of the HIV seropositive patients were non diabetic. 3 (60%) out of 5 cases had CD4 count <350 cells/mm<sup>3</sup> and the rest 40% had >350 cells/mm<sup>3</sup>.

## DISCUSSION

The present study was conducted in the Department of Tuberculosis and Chest Diseases, Amritsar to

study the percentage of HIV seropositivity in smear positive tuberculosis cases.

In the present study, out of 150 sputum smear positive tuberculosis patients screened for HIV infection, 5 (3.33%) were HIV seropositive which is lower or equal than the other Indian studies. In 2017, 10,97,755 TB patients (75% of total TB patients notified) were tested for HIV, 3% among whom were diagnosed as HIV positive and were offered access to HIV care.<sup>4</sup> The published reports about seroprevalence of HIV among tuberculosis patients give highly variable rates worldwide. Eriki et al,<sup>[15]</sup> found that 66% newly diagnosed tuberculosis patients in Kampala (Uganda) were HIV seropositive. Eilhot et al reported 60% seroprevalence among tuberculosis patients in Zambia. But, Onorato and McCray,<sup>[16]</sup> had reported that 3.4% of the 3,077 tuberculosis patients had HIV co-infection in U.S.A.

In India too, wide variations in HIV seroprevalence among tuberculosis patients have been observed. Solomon et al,<sup>[17]</sup> found 0.77% of tuberculosis patients HIV positive, in 1991 and a higher seroprevalence, in 1993 (3.35%). Banavaliker et al,<sup>[18]</sup> found 0.5% HIV seropositive in hospitalized tuberculosis cases while Jayaswal et al,<sup>[19]</sup> reported 4.0% seroprevalence in Military Hospital, Pune. Mohanty & Basheerhad,<sup>[20]</sup> reported an alarming increase of HIV infection, from 2.56% in 1988 to 10.15% in 1993-94, among hospitalised tuberculosis patients in Mumbai, while Anuradha et al,<sup>[21]</sup> reported 12 of 3,071 (0.4%) tuberculosis cases positive for HIV from Tuberculosis Research Centre, Chennai. In one of the study confined to Delhi state, covering 2,361 tuberculosis patients, the seroprevalence found (0.68%) was no different from the observation made by Jain et al.<sup>[22]</sup>

In India, the prevalence of HIV among TB patients was generally high in some areas, such as Mumbai(30%), Pune (28.75%) and Mangalore (21%), compared with areas with a low prevalence, such as New Delhi (0.68%), Jammu and Kashmir (1.6%), Aligarh (2.8%), Indore (4%), Tamil Nadu (4.7%) and north eastern states (12.3%). In India the seroprevalence of HIV infection is 1-2% (Laal et al) while that of TB is high at 40% (Narain).<sup>[23]</sup>

The increased percentage of seropositivity in our study was due to two reasons. Firstly, in place of random screening, only TB cases were included in the study though they were only smear positive tuberculosis cases where the prevalence of HIV seropositivity is less. Secondly, study included more of high risk populations especially prisoners. Also, there is a large population in Punjab where the drug abuse is high.

Intravenous drug abuse was the main risk factor in the present study, found in 3 (60%) patients of HIV seropositivity followed by heterosexual promiscuity found in the rest two (40%) of them in contrast to the results found by Mohanty et al,<sup>[20]</sup> and Arora et al

where heterosexual promiscuity was the major risk factor. It is likely that patients from our study were reluctant to reveal about their heterosexual relation with more than one person due to the prevailing social values, which discourage polygamy and homosexuality. There was no history of blood transfusion or history of HIV seropositivity in wives of these cases.

Tubercular coinfection is common in HIV infected and more so with falling CD4 cell level. In our study, 60% cases had CD4 count >350 cells/mm<sup>3</sup> and the rest 40% had CD4 count <350 cells/mm<sup>3</sup>. Among 5 HIV seropositive patients detected in 150 smear positive tuberculosis cases, bacillary grading decreased in a linear fashion with declining CD4 count, supporting the findings of various studies. A potential underlying mechanism is that waning immunity is associated with reduced pulmonary immunopathology with consequent liberation of lower concentrations of bacilli into the airways.<sup>[24]</sup> Although HIV coinfection is well recognized to be associated with higher proportions of smear-negative PTB and EPTB compared to HIV-uninfected cases, but in our study, we have taken all the smear positive tuberculosis patients, so we are unable to make the correlation between CD4 count and the sputum positivity.

## CONCLUSION

So, in all, the HIV seropositivity detected in 150 smear positive tubercular cases was 3.33% which is more than the prevalence seen in most of the northern states and lower than the southern and north eastern states of India.

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